Before we actually look at an antibody, I would like to introduce you to the concept of modeling, because what I've done with these antibodies is essentially, I've made all kinds of models of them, foam board and pictures and pipe cleaners and all kinds of strange things to give you an idea of how an antibody is structured. Now, as you can see from the screen, there are more than one kind of model you can have. And so up here, the first model we have is that of a DNA molecule. And this particular one is a three dimensional model, a space filling model, and it gives you an idea what the molecule might in a sense look like, but it's not a DNA molecule. So when we produce a model, we are producing some form of abstraction that represents what we want to pay attention to if we want to discuss certain aspects of structure or function. Now, you're probably familiar with physical models and all kinds of other situations. I'm sure you've looked at house plans. That's a model. It's not the whole house. The US government has three dimensional models of aircraft carriers and to scale all the stuff that goes on them, so that way they can load up the aircraft carrier and they won't find out at some critical moment that some wing is 1ft too long. So you can use physical models we'll see to play with. When I get done introducing the section, the next thing we're going to look at is a model of signaling. And I'm going to have a model that I hope is kind of fun. But again, it doesn't completely give you the full complexity of signaling, but it gives you some sort of introduction and insight and feel for what's going on, as one element of a cell interacts sequentially with other elements to produce a response. In addition to some of these traditional models, what you may not realize is that many of the lab animals that we work on are also models. When we first started looking at biological processes, we looked at them in organisms that were in a sense, simpler. Virus, which isn't even an organism. Bacteria, which are small and can be grown in vats, yeast cells, and these things are still used as models and something called dictyostelium, the cellular slime mold. So a dictyostelium and a yeast cell are relatively simple, nobody cares if you kill them, okay? And many processes in biology are very similar in yeast indictyostelium and in humans. However, the more complex the process is, the more similar the organism is that you need to use to model it. In humans, there are some things in psychology that you have to use, well, even some form of primate. And primates are really tricky to work with. You have to be very careful with them. Not only do you have to keep them healthy, you have to keep them happy. And otherwise they get neurotic. So we often try to find the simplest organism we can use to have a process that's similar to that that goes on in humans. So many processes are modeled in C Elegans, the round worm. And here at rice, we use C Elegans as a model system to study a number of developmental events. Fruit flies, Drosophila. And so here you see a picture of Drosophila. It's, again, small, and nobody cares if you kill a lot of them. For plants, we have arabidopsis. Arabidopsis has been referred to as the fruit fly of the plant world. We have a lot of information on plants in general that we've gotten by studying arabidopsis. When we need to get something that's a little closer to humans, we will often use fish. So here's a zebrafish, or we'll use mice. Now you've finally got something that's really, really cute. So if you're going to work with a mouse, you have many kinds of protocols that will prevent you from being mean

to your mice or having them suffer. But in any event, mice are probably the best models we can use if we're going to look at immunology, on the other hand, there are many processes that we look at that we can use other organisms, and we can and do. So. You know, what makes a good model a good model? Well, in general, you have to understand that a model is a stand in for what you want to study. And it's a stand in that one would hope works roughly the same way, but maybe a little bit simpler and cheaper and easier to manipulate. So I think you can see that while nobody really objects to growing bunches of fruit flies and then throwing them away, even with mice, you're not supposed to use any more than you absolutely have to. And I think most of you can see that most people would much rather have you experimenting on mice and getting things right before you do anything to human beings. So a good model is something that allows you to manipulate and play with things with a lower risk. That's the whole point of that aircraft carrier model. Another example of this is that there is a three dimensional scale model of the Mississippi river so that you can model flooding without taking out an entire city. And so having a system that allows you to play and manipulate at low cost is something that a model can supply. Another thing that a model can supply is a comprehensible scale. So the first model we had, a DNA molecule, is much, much bigger than the real thing because you can't really see the real thing in any detail. And so you've got a model that shows you the structure at a scale you can comprehend. To flip that around, another way of showing you things at a comprehensible scale would be if you go to the planetarium and you see a scale model of the solar system, you know, the solar system itself is way too huge for you to really grasp. But if I do it in a smaller scale, you can see what's going on. So that's modeling. And also as an extension of this, any good theory is really a model. It is a model in the sense that a really good theory is not the real thing. It's more abstract, it's more simple. It's something that you could, for example, program the implications into a computer and test to see how well it captures reality. And so a good model is something that helps you understand and play with concepts and then apply those concepts back to the real thing. So in the next part of this lecture, we're going to look at a kind of fun model and see it applied, as we'll see, to signaling in cells. So we've looked at the characteristics of a good model, and I'm going to start showing you some examples of models. And the first model I'm going to show you, I didn't make myself. This is a mouse trap game, and you may have played with it as a kid, but it is an example of what we would call a Rube Goldberg apparatus. And Rube Goldberg was a cartoonist who used to sort of design funny mechanical sequences whereby you had a signal at one end and a response at the other and an unnecessarily complicated series of events in between. So here I'm going to take this and I'm going to put in a signal, and I'm going to set off a ball, which sets off another ball and ultimately puts down the mouse trap. Now, what is this a model of? This is kind of a model of the signaling sequences that you find in the interior of the cell. Is it a good model? Well, it gives you an idea of how many complicated steps there might be from your initial stimulus to ultimately your response, in this case, the dropping of the cage. On the other hand, it's not a perfect model. The inside of your cell looks nothing like this. And more to the point, we had a straightforward sequence of events from turn to boot to ball to second ball to jump to down with a mousetrap. In a real cell, you will have situations where things

just don't necessarily go from a to b. There will be other inhibitory signals that modulate it. A signal may branch, like a chain of dominoes into two separate signals. And we'll look at some examples of this in the cell. But always keep in mind, we're looking at a complicated series of signals, and it's easy to get lost in the details. Incidentally, my favorite Rube Goldberg is something that you can pull up on the web. It's called this too shall pass, and it is a video with the most spectacular sequence of Rube Goldberg events anywhere. All right, so in the meantime, let's go take a different model. This is my model of a toe like receptor, and we're going to see how these signals work more or less in a membrane. So if I take my toe like receptor, I will see that it is embedded in the plasma membrane, and that means that it has an outside part. Well, the outside part will receive a signal. And so this is a very, very common theme in signaling that there will be something outside the cell that triggers or signals to a part of the cell, a protein that's sticking out. In this case, we have something like the signature of a pathogen. On the other hand, when we look later on at hormones and paracrine factors, we'll see that sometimes these signals are part of a chemical conversation between two cells. In those cases, a lot of times it causes two of these molecules to get together. But whether we have one signal in one molecule or a signal that brings together two of these molecules, the next thing that happens is we have a shape shift, a conformational shift in this molecule, and so we will transduce the signal from the outside to the inside. Now, once you've done that, that's when you go into a series of Rube Goldberg type mechanisms. And ultimately what usually happens is you stick phosphates on and off things, and eventually you will get into the nucleus and make changes in the transcription or expression of the DNA. So this Rube Goldberg apparatus is a way of representing the fact that it's a long, long way from the outside signal to the ultimate changes in gene expression, and that this involves a long series of changes in the DNA. So that's the good part of this molecule or model. The again, inadequate part is that it doesn't really, of course, capture the complexity of what happens in that pathway in the interior. We will see that there are many different kinds of signals that can kick off this pathway. There are many different kinds of receptors. Some of them act in isolation, some of them act by coming together. There are huge numbers of different pathways in the interior, and they involve putting things together and in many cases, taking phosphates on and off of molecules. The ultimate, but not the only, kind of effect of this will be to make a change in molecules, protein molecules that bind to DNA. You can call those transcription factors because they change the transcription pattern of the DNA, upregulating some genes and downregulating others.